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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,620	02/04/2004	Jonathan M. Graff	UNI919/4-8US	9412

7590 07/10/2007

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EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

MAIL DATE	DELIVERY MODE
07/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/771,620	GRAFF ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *27 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above claim(s) *13, 15-55,57, 59, and 60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,14,56,58 and 61-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed April 27, 2007 in response to the Office Action of October 18, 2007, is acknowledged and has been entered. Claims 1, 5, 9, and 58 have been amended and new claims 61-65 have been added.

2. Claims 1-12, 14, 56, 58, and 61-65, drawn to nucleic acid based methods for diagnosing breast cancer in a subject and SEQ ID NO: 3 and 4 and the species (A) FLJ20174, (B) breast cancer (C) amplifying the nucleic acid are currently under consideration.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-12, 14, 56, and 58 remain rejected and claims 61-65 are rejected under 35 USC 112 for the reasons previously set forth in section 14 of the Office Action of October 18, 2007.

Applicants argue that the claims do not require distinguishing between breast cancer and ovarian cancer, but instead are drawn specifically to diagnostic methods that are "indicative of breast or ovarian cancer in the subject." Thus, the claims are not directed to a definitive diagnosis of breast cancer, but rather diagnostic methods that are indicative of breast cancer, and suggest that further analysis of the subject may be warranted. This type of diagnostic method is particularly valuable for identifying early-stage cancer, which typically is more treatable, to help increase long-term survival of the subject. Applicants argue that, for example, a blood sample of a subject may be initially analyzed for upregulation in the expression of FLJ20174. If such an

upregulation is identified, a tissue such as breast cancer tissue may be obtained from the subject for further analysis (since FLJ20174 is upregulated in breast cancer tissue). One of skill in the art would understand that other analyses, such as radiographic imaging of the breast, can be conducted to confirm diagnosis.

Applicants' arguments have been carefully considered, but have not been found persuasive. As the claims are drawn to the diagnosis of breast cancer as claimed and contemplated, not methods that are indicative of breast cancer or methods that comprise identifying early-stage cancer or radiographic imaging of the breast, Applicants are arguing limitations not found in the claims and, thus, the arguments are not found persuasive.

Applicants argue that based on the reasoning presented by the Action, prediction of one specific type of cancer by detecting upregulation of the expression of a particular gene would be enabled only if it occurred for one specific type of cancer, e.g., breast cancer. The Action argues: "Thus, undue experimentation would be required to demonstrate that the FLJ20174 RNA expression pattern is solely diagnostic for breast cancer and not for other cancers by, for example, determining the FLJ20174 RNA expression pattern is a larger set of ovarian tumors or by determining the FLJ20174 RNA expression pattern in multiple other tumor types." Action, p. 13. Applicants argue that such an argument is untenable. Applicants argue that the many genes have been shown to be upregulated in more than one cancers. Just because routine subsequent specific tissue testing, imaging, etc. is conducted to confirm diagnosis in no way reduces the fact that prediction of a specific type of cancer by detecting a particular marker is enabled.

Applicants' arguments have been carefully considered, but have not been found persuasive. The fact, as Applicants have stated, that many genes are upregulated in more than

one cancer, as FLJ20174 appears to be, supports Examiners argument as previously set forth that comparing the expression pattern of the FLJ20174 nucleic in a sample to samples from non-cancerous tissues alone would not be diagnostic for breast cancer on its own. Furthermore, Applicants are arguing limitations not found in the claims, i.e. routine subsequent specific tissue testing.

Applicants argue that as the Action notes, FLJ20174 is overexpressed in 75% of ductal breast carcinomas when compared to normal breast tissue, and the average expression level of FLJ20174 is about 5.5 fold higher in breast cancer samples than in normal breast tissue. Action at 10-11. Applicants argue that because FLJ20174 is overexpressed in most ductal breast carcinomas, it is a valid marker for diagnosing breast cancer.

Applicants' arguments have been carefully considered, but have not been found persuasive because, as set forth above and previously, FLJ20174 is not solely expressed and upregulated in breast cancers, thus comparing the expression pattern of the FLJ20174 nucleic acid in a sample to samples from non-cancerous tissues alone would not be diagnostic for breast cancer on its own.

Applicant's arguments have not been found persuasive and the rejection is maintained.

5. Claims 1-8, 14, 56, and 58 remain rejected and claim 65 is rejected under 35 USC 112 for the reasons previously set forth in section 15 of the Office Action of October 18, 2007.

Applicants argue that with respect to claims directed to FLJ20174 nucleic acids, the specification provides sufficient guidance to allow one of skill in the art to use the claimed methods as claimed. As the Action notes, the specification defines "FLJ20174 nucleic acid sequence" as SEQ ID NO: 3 and SEQ ID: 4 and homologs, mutations or variants of those

sequences found in a subject. This definition, however, does not encompass a "whole universe" of FLJ20174 nucleic acid molecules as the Action contends. The BioTech Life Science Dictionary defines "homologous genes" as "A pair of genes from different but related species which correspond to each other and which are identical or very similar to each other." (http://biotech.icmb.utexas.edu/search/dict-search.html; accessed March 15, 2007). Thus, FLJ20174 nucleic acid homologs are identical or very similar sequences found in other species. Mutations or variants are the various FLJ20174 nucleic acid sequences or alleles found within a species. As the Action notes, the specification provides two FLJ20174 sequences, SEQ ID NO: 3, the wild type isoform of FLJ20174, and SEQ ID NO: 4, a splice variant of FLJ20174 that share substantial sequence identity with wild type FLJ20174. Thus, the specification provides an example of a variant FLJ20174, illustrating that mutations and variants, as with homologs, would be easily identifiable by one of skill in the art and show substantial sequence identity to wild type human FLJ20174, as embodied in SEQ ID NO: 3.

Applicants' arguments have been carefully considered, but have not been found persuasive. Applicants are arguing limitations not found in the claims as the claims are not limited only to homologs of SEQ ID NO: 3 or 4 and the mutations or variants of SEQ ID NO: 3 or 4 are not limited by the claims or the teachings of the specification. Furthermore, Applicants definition of homologous gene does not sufficiently limit homologs to enable the full scope of the claims for the reasons previously set forth. Thus, the teachings in regard to SEQ ID NO: 3 and 4 are not sufficient to enable all of the mutations and variants of these sequences contemplated for FLJ20174 for the diagnosis of breast cancer.

In regard to new claim 65, it is noted that the specification teaches that naturally-occurring allelic variations of those sequences can exist in a population, including splice-variants, insertions, deletions and point mutations in the CXCL9 and FLJ20174 nucleic acid sequence that result in the expression of an altered gene product. Thus for the reasons set forth above and in section 15 of the Office Action of October 18, 2007 claim 65 is also rejected.

Applicant's arguments have not been found persuasive and the rejection is maintained.

6. Claims 1-9, 14, 56, and 58 remain rejected and claim 65 are rejected under 35 USC 112 as lacking an adequate written description for the reasons previously set forth in section 17 of the Office Action of October 18, 2007.

Applicants argue that this rejection appears to be related to the enablement rejections. To the extent that this is the case, Applicants request reconsideration of the rejection in light of the arguments made above. Additionally, Applicants note they have provided SEQ ID NO: 3 and SEQ ID NO: 4 and have provided working examples demonstrating changes in expression of SEQ ID NO: 3 and SEQ ID NO: 4 as diagnostic for cancer. Moreover, by disclosing the entire SEQ ID NO: 3 and SEQ ID NO: 4, Applicants have provided all possible nucleic acids comprising 30 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4 and placed them fully in possession of one of skill in the art. In addition, as already discussed by Applicants herein, the odds of such a 30 contiguous nucleotide sequence occurring randomly is 1 in 1.5×10^{18}. To the extent that this rejection is not related to the enablement rejection above, Applicants request clarification of the rejection. .

Applicants' arguments have been carefully considered, but have not been found persuasive. As set forth previously, and as the claims are not limited to SEQ ID NO: 3 and/or 4, the changes in expression of SEQ ID NO: 3 and 4 in breast cancer are not sufficiently representative of all the homologs, variants or mutations of SEQ ID NO: 3 and 4 contemplated for the FLJ20174 nucleic acid in the specification and thus do not provide an adequate written description of the claimed method which compare the expression of FLJ20174 to in different samples to diagnose breast cancer.

In regard to new claim 65, it is noted that the specification teaches that naturally-occurring allelic variations of those sequences can exist in a population, including splice-variants, insertions, deletions and point mutations in the CXCL9 and FLJ20174 nucleic acid sequence that result in the expression of an altered gene product. Thus for the reasons set forth above and in section 17 of the Office Action of October 18, 2007 claim 65 is also rejected.

Applicant's arguments have not been found persuasive and the rejection is maintained.

New Grounds of Rejection

7. Claims 62-64 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitations of a nucleic acid comprising 25 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4, a nucleic acid comprising 20 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4, and a nucleic acid comprising 15 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4 claimed in Claims 62-64 have no clear support in the specification and the claims as originally

filed. Examiner's review of the specification did not reveal support for the newly added limitations.

Applicants pointed to support for new claims 62-64 in paragraph 57. A review of the specification at paragraph 57 discloses support for: naturally-occurring allelic variations of those sequences can exist in a population, including splice-variants, insertions, deletions and point mutations in the CXCL9 and FLJ20174 nucleic acid sequence that result in the expression of an altered gene product. Such variations can be oncogenic or benign in nature. Methods for detecting and determining the effects of such allelic variations are well-known to those of skill in the art.

The suggested support is not found persuasive because there is nothing in the specification to suggest a nucleic acid comprising 25 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4, a nucleic acid comprising 20 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4, and a nucleic acid comprising 15 or more contiguous nucleotides of SEQ ID NO: 3 or SEQ ID NO: 4

Applicant is invited to submit evidence pointing to page and line number in the specification wherein support for the newly added limitation can be found. The subject matter claimed in claims 47-58 broadens the scope of the invention as originally disclosed in the specification.

8. No claims allowed.

9. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to

the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal form, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

10. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

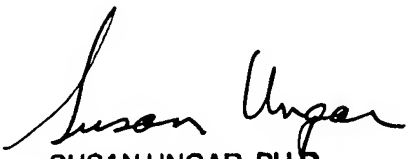
A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL

AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0890. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

PJR